DEPARTMENT OF HEALTH AND HUMAN SERVICES

MEMORANDUM OF CONFERENCE
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Participants:

DNA Plant Technology Corp. (DNAPT):

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FDA:

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Subject: Delayed-ripening tomato

Introduction

This meeting was intended to bring to closure DNAPT's consultation started in March 1993 (see SBJ 1319). DNAPT had previously submitted (September 16, 1994) a draft summary of the safety assessment of their delayed-ripening tomato line 1345-4.

Introduced Genetic Material

DNAPT described the identity and function of the genetic material introduced into the tomato using the *Agrobacterium* transformation system (summarized in the summary document). DNAPT presented DNA mapping and segregation studies which allowed them to conclude that they have 1) properly identified the sequences that were inserted into the plant genome, 2) ascertained that no vector or non-T-DNA sequences were found in the plant genome, 3) determined that three copies of the T-DNA were inserted at a single insertion site, and 4) determined that the insert remained stably integrated through successive generations.

Identity and Function of Expression Products Encoded by the Inserted Genetic Material

The only new protein that is expressed in the transgenic tomato is the enzyme aminoglycoside 3'-phosphotransferase II (APH(3')II), which is encoded by the *kan*^{r} (*nptII*) gene originally isolated from transposon Tn*5* isolated from *E. coli*. The *kan*^{r} gene is used as a selectable marker. DNAPT stated that they carried out an open reading frame (ORF) analysis of the entire inserted DNA and that, while the analysis showed the presence of some potential ORFs other than the *kan*^{r} and the truncated ACC synthase ORFs, they could detect no transcripts corresponding to the ORFs in the plants using appropriate double-stranded probes.

The insert also contains a fragment of the aminocyclopropane carboxylic acid (ACC) synthase gene in the sense orientation. According to DNAPT, the ACC synthase gene fragment is transcribed but not translated into a protein product; rather, transcription of the truncated gene causes suppression of the endogenous ACC synthase (Transwitch™ gene suppression technology). ACC synthase is the enzyme which catalyzes the rate-limiting conversion of S-adenosylmethionine (SAM) to ACC, the immediate precursor to ethylene. According to DNAPT, suppressing ethylene synthesis in the transgenic tomatoes causes a delayed-ripening phenotype; these tomatoes ripen normally when an external source of ethylene is applied.

Safety of the Introduced Protein

The new varieties contain only one added protein, namely APH(3')II. DNAPT noted that the safety of this protein in the development of new varieties of tomatoes has been addressed previously (21 CFR 173.170 and 21 CFR 573.130). Nonetheless, DNAPT presented data to show that the protein was expressed at very low levels (ranging from 0.72 to 2.36 ng per gram fresh weight of tomato).

Compositional Analysis

Endogenous toxicants

DNAPT stated that tomatine levels were measured in their transgenic line 1345-4, parental line 91103-114, and a commercial fresh market variety, Sun J, grown in Southern California. According to DNAPT, tomatine levels in the transgenic tomato are unchanged from the parental variety or the traditionally-bred tomato variety (see summary document).

Concentration and Bioavailability of Important Nutrients

DNAPT noted that tomatoes make important contributions to dietary intake of vitamins A and C but are not significant sources of other dietary nutrients. DNAPT has therefore measured vitamins A and C in their transgenic and parental lines, hybrids derived from the parental line, and a non-parental commercial variety, obtained from three growing regions of the U.S. DNAPT stated that vitamin A and vitamin C levels in ripe fruits of all analyzed lines are within the ranges typical for tomatos (see summary document).

Conclusions

DNAPT has concluded, in essence, that the delayed-ripening tomato variety they have developed is not significantly altered within the meaning of 21 CFR 170.30(f)(2) when compared to tomato varieties with a history of safe use. At this time, based on DNAPT's description of its data and analysis, the agency considers DNAPT's consultation on this product to be complete.

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Compositional Analysis

Based on the nature of the genetic modification, it is expected that cotton lines 757 and 1076 would not differ significantly in composition from other cotton varieties. To confirm this expectation, Monsanto analyzed the composition of cottonseed oil, and cottonseed meal obtained from lines 757, 1076, and a parental control line.

Based on their analyses of line 531, Monsanto has concluded that cotton linters derived from their cotton lines 757 and 1076 are not materially different from cotton linters derived from other cotton varieties. They noted that the composition of linters is >99% cellulose; and because of the extensive processing prior to food use, fiber used for food is not expected to contain any detectable genetic material or protein.

Monsanto has concluded that cottonseed derived from their cotton lines 757 and 1076 is not materially different from cottonseed derived from other cotton varieties in their content of: protein, lipid, carbohydrate, ash, moisture, fatty acid profile, amino acid composition, or calories. Moreover, Monsanto has concluded that the levels of gossypol, aflatoxin, and cyclopropenoid fatty acids in cottonseed produced by lines 757 and 1076 are similar to levels observed in cottonseed produced by the parental line.

Monsanto has concluded that cottonseed oil derived from their cotton lines 757 and 1076 is not materially different from cottonseed oil derived from other cotton varieties in the content of fatty acids (14:0, 16:0, 16:1, 17:0, 18:0, 18:1, 18:2, 18:3, 20:0, and 22:0), as well as, several cyclopropenoid fatty acids (sterculic, dihydrosterculic, and malvalic), and α-tocopherol levels.

Finally, Monsanto has concluded that cottonseed meal derived from their cotton lines 757 and 1076 is not materially different from cottonseed meal derived from other cotton varieties.

Compositional Analyses

The firms performed compositional analyses on sugar beets obtained from a number of field trials conducted in both the U.S. and Europe. The firms conducted proximate analyses on top and root samples for ash, crude fiber, crude protein, dry matter, soluble carbohydrates. In addition, crude fat was measured in tops, and acid detergent fiber and neutral detergent fiber were measured in roots. The firms report that all values are comparable between the control and transgenic sugar beet and fall within literature ranges. The firms also analyzed processed sugar beet (brei) for sucrose, sodium, potassium, amino nitrogen and invert sugar levels. The firms report that all values are comparable between the control and the transgenic sugar beet and within the literature value ranges.

Saponins are triterpenoid glycosides that have a broad biological activity and occur naturally in numerous food and feed crops including sugar beets. The firms conducted analyses for saponins in root and top tissues from the transgenic and control sugar beets. From their analyses, the firms conclude that the levels of saponins in their transgenic sugar beet are not altered relative to commercially available varieties, and the levels of saponins in the transgenic sugar beet fall within the reported literature range for traditional sugar beet lines.

Conclusion

Monsanto and Novartis have concluded that their transgenic sugar beet line 77 is not materially different in terms of food safety and nutritional profile from sugar beet varieties currently on the market. At this time, based on Monsanto's and Novartis' description of their data and analyses, the Agency considers the consultation on their glyphosate-tolerant sugar beet line 77 to be complete.

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